

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
19 December 2002 (19.12.2002)

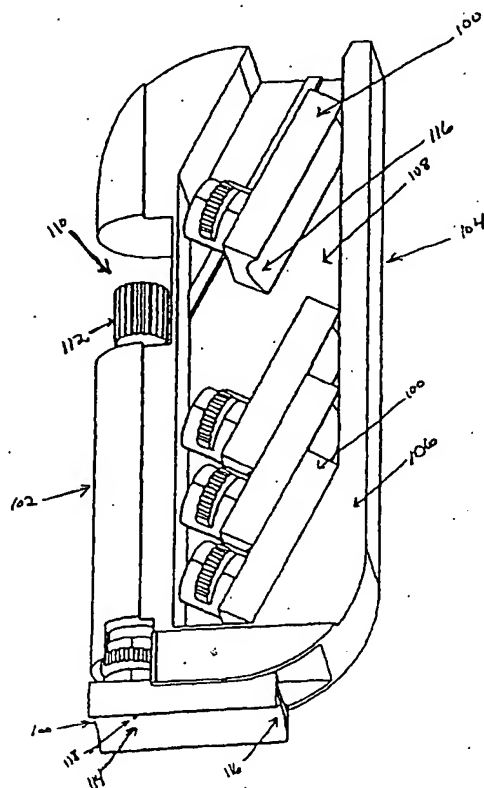
PCT

(10) International Publication Number
WO 02/100252 A2

- (51) International Patent Classification: A61B
- (21) International Application Number: PCT/US02/19054
- (22) International Filing Date: 12 June 2002 (12.06.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/298,056 12 June 2001 (12.06.2001) US
- (63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 60/298,056 (CIP)
Filed on 12 June 2001 (12.06.2001)
- (71) Applicant (for all designated States except US): PELIKAN TECHNOLOGIES, INC. [US/US]; 1072 East Meadow Circle, Palo Alto, CA 94303 (US).
- (72) Inventors; and
(75) Inventors/Applicants (for US only): ALDEN, DON [US/US]; 1312 NELSON WAY, SUNNYVALE, CA 94087 (US). FREEMAN, Dominique, M. [GB/US]; 4545 La Honda Road, La Honda, CA 94020 (US). LUM, Paul [US/US]; 690 Templebar Way, Los Altos, CA 94022 (US). DRBAL, Vladimir [US/US]; Suite 4812, 400 Davey Glen Road, Belmont, CA 94002 (US). TEMPLIN, Catherine, K. [US/US]; 291 La Cuesta Drive, Portola Valley, CA 94028 (US). BOECKER, Dirk [DE/US]; 1652 Casteilleja Avenue, Palo Alto, CA 94306 (US).
- (74) Agents: SEIDMAN, Stephanie, L. et al.; Heller Ehrman White & McAuliffe, 4350 La Jolla Village Drive, 7th Floor, San Diego, CA 92122-1246 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

[Continued on next page]

(54) Title: BLOOD SAMPLING APPARATUS AND METHOD



(57) Abstract: Blood samples can be collected without substantial contamination from ambient air, such that the blood sample may be analysed accurately for gaseous components such as oxygen and carbon dioxide. An embodiment of the device has integrated actuation, lancing, and sample acquisition components, which in some embodiments are miniaturized and/or disposable.

WO 02/100252 A2



LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,

IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

Published:

- without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

BLOOD SAMPLING APPARATUS AND METHOD

TECHNICAL FIELD

Biochemical analysis of blood samples is an important diagnostic tool for determination of patient status. Analysis of a blood sample for glucose level can provide a powerful tool for diabetics who require tight control of blood glucose levels in an effort to minimize the deleterious long-term effects of the disease. At this time, noninvasive blood analysis technology does not provide the accuracy and specificity required for clinical testing, so that test samples are mainly derived from blood, interstitial fluid, urine or saliva. Many point of care tests are performed directly on capillary whole blood, which is typically obtained by making a small incision on a finger using a hand-held lancing device. The hand-held lancing device usually includes a lancet that is rapidly displaced to penetrate the finger, creating a small wound from which a blood droplet forms on the surface of the skin after the lancet has retracted from the incision. Generally the blood droplet is placed on a sample assay strip, and the sample assay strip is analyzed using a measurement device.

BACKGROUND ART

The process of acquiring and testing a blood sample using these conventional devices can be painful and often involves numerous steps, the outcome of which is to reduce patient compliance with the frequent self testing regimens required for disease management. In addition to the pain and the paraphernalia required for self-testing, the success rate of obtaining an adequate blood sample is not 100%. The success rate can be affected by the reproducibility of the lancing technique used (due to variation in skin hydration and thickness, calluses, etc.) as well as the ability to obtain the blood droplet from the incision. Current industry standard lancet and lancing devices can have as low as a 50% success rate in generating a blood sample from the fingertip. The diabetic wishing to adhere to the optimal 5 – 6 times a day self testing regimen would, in essence, need to lance themselves an average of 10 – 12 times just to obtain the blood

samples required. The more successful lancing devices are, in reality, about 80 – 90% successful.

What has been needed is an improved method for sampling and analyzing bodily fluid which is seamless and cost-efficient resulting in a simplified procedure for extraction and analysis of blood samples at the patient's side.

DISCLOSURE OF INVENTION

Embodiments of the invention allow acquisition of the blood sample seamlessly, that is, without substantial contamination from ambient air, such that the blood sample may be analyzed accurately for gaseous components such as oxygen and carbon dioxide.

Embodiments of the invention have integrated actuation, lancing, and sample acquisition components, which can optionally be miniaturized and/or disposable. Sampled blood can be acquired and transported to an analysis or storage device without substantial contamination by ambient air.

Embodiments of the disposable sample acquisition module can collect a sample in an integrated fashion. In the operation of some embodiments, a finger of the user is placed on the sampling site, where the finger remains throughout the integrated lancing and sample collection process.

In certain embodiments of the invention, in order to facilitate adequate sample volume for analysis, three approaches are described, of which a single approach might be used, or any two or all three approaches may be used in concert. The first approach describes a surface treatment of the support material to engender a difference in wetting ability. The second describes an active pumping device in addition to capillary forces for drawing the blood into the sample reservoir and for dispensing blood from the reservoir to additional sites. The third includes the use of a device which compensates for an inadequate sample volume in the first sample reservoir by isolating the first sample reservoir and triggering a second lancing and acquisition step to fill a second "back-up" sample reservoir.

One embodiment of the invention is directed to a miniature lancing and blood sampling device. Analysis of small blood volumes (less than about one milliliter) is achieved by the collection and the transportation of the blood micro sample to sample

storage area or analytical sites. Sampled blood can be transported reliably and without excessive turbulence, cavitation or damage to the cellular components. Furthermore, analyte detection is achieved via the blood samples reliably reaching and saturating the appropriate test sites. Embodiments of the invention provide techniques for extracting a sample of human blood for the measurement of one or more of its constituents, such as might be used for routine monitoring of a chronic condition such as diabetes mellitus. The techniques of embodiments of the present invention simplify the extraction and transfer of the blood sample, and reduce the inconvenience of the process. The techniques can be advantageously used in, for example, blood glucose monitoring as explained above.

BRIEF DESCRIPTION OF DRAWING

The objects, advantages and features of this invention will be more readily appreciated from the following detailed description, when read in conjunction with the accompanying drawing, in which:

Figure 1 illustrates a blood sampling system having features of the invention.

Figure 2A is a cross section view through line A of Figure 2B, which shows some details of a sample acquisition module according to embodiments of the invention.

Figure 3 schematically depicts a portion of the sample acquisition module illustrating an alternate embodiment of the sample reservoir.

Figure 4 depicts a portion of the disposable sample acquisition module surrounding the sampling port.

Figures 5A, 5B, and 5C show in section view one implementation of the lancet driver at three different points during the use of the lancet driver.

BEST MODE FOR CARRYING OUT THE INVENTION

Patents U.S. 3,030,059, U.S. 3,626,929, U.S. 4,360,016, U.S. 4,608,997, U.S. 4,622,974, U.S. 4,627,445, U.S. 4,637,403, 4,648,408, U.S. 4,653,513, U.S. 4,873,993, U.S. 4,883,068, U.S. 4,895,147, U.S. 4,920,977, U.S. 5,047,044, U.S. 5,871,494, U.S.

5,971,941 and WO 97/42882 are hereby incorporated by reference in their entirety herein.

Further aspects and advantages of the invention will be set forth in part in the description which follows, and in part will be obvious from the description, or may become readily apparent through practice of the invention. It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

"Integrated" as used herein means that two or more functions are conducted without intervention by the user: the "integrated" housing contains the mechanism for a plurality of functions, e.g., reproducible lancing, blood sample storage, and (optionally) analysis, the combination of functions occurring as the result a single initiating act by the user (i.e. each function does not have to be separately initiated). The "initiating act" is an action performed by the user which results in a plurality of actions (e.g. blood collection, storage, and analysis) being performed by the blood sampling device without further action required of the user. In the context of a combined lancet driver/sample acquisition module, integrated means that actuation of the lancet driver, lancing of the skin, and sample collection and storage all may occur as the result of a single simple motion (the initiating act) by the user, such as pressing the device against the skin to be sampled. In the context of a sample acquisition module which is configured to be disposable and attached to a reusable lancet driver during use, integrated means that lancing of the skin, sample collection, and sample storage all may occur as the result of a single simple motion by the user, such as pressing the device against the skin to be sampled. If a device is "configured to allow integrated steps A, B, and C", then steps A, B, and C all follow as a result of a single initiating action. "Reproducible" in this context means that the lancing is controlled, having adjustable depth, preload force, and (optionally) opportunity for multiple lancing to assure a sufficient blood sample is obtained. "Preload force" is a measure of the amount of force which must be applied to the skin of the user by the apparatus before triggering the firing of the lancet, and "adjustable preload force" allows the user to select the amount of preload force, in such a manner that the selected amount of preload force will be consistently applied in each successive use of the apparatus unless the user re-adjusts the preload force setting.

“Seamless” as used herein means without substantial exposure to contaminating air: “seamless sampling” thus includes obtaining a blood sample, storing the sample, and (optionally) subjecting the blood sample to analysis without substantial contamination from ambient air. “Substantially” or “substantial” in this context means that the analysis results obtained from the blood sample according to the method or using the apparatus described herein do not deviate by more than about 10%, more preferably 5%, from analysis results obtained using methods that are conventional in the art for analyzing blood samples without contamination from ambient air. “Optional” or “optionally” means that the subsequently described circumstance may or may not occur, so that the description includes instances where the circumstance occurs and instances where it does not. For example, if a device optionally contains a feature for analyzing a blood sample, this means that the analysis feature may or may not be present, and, thus, the description includes structures wherein a device possesses the analysis feature and structures wherein the analysis feature is not present.

“Testing means” refers to any use, singly or in combination, of chemical test reagents and methods, electrical test circuits and methods, physical test components and methods, optical test components and methods, and biological test reagents and methods to yield information about a blood sample. Such methods are well known in the art and may be based on teachings of, e.g. Tietz Textbook of Clinical Chemistry, 3d Ed., Sec. V, pp. 776-78 (Burtis & Ashwood, Eds., W.B. Saunders Company, Philadelphia, 1999); U.S. Pat. No. 5,997,817 to Chrismore et al. (Dec. 7, 1999); U.S. Pat. No. 5,059,394 to Phillips et al. (Oct. 22, 1991); U.S. Pat. No. 5,001,054 to Wagner et al. (Mar. 19, 1991); and U.S. Pat. No. 4,392,933 to Nakamura et al. (July 12, 1983), the teachings of which are hereby incorporated by reference, as well as others. The testing means may include sensors in the sample reservoir which test electrochemical properties of the blood, or they may include optical means for sensing optical properties of the blood (e.g. oxygen saturation level), or they may include biochemical reagents (e.g. antibodies) to sense properties (e.g. presence of antigens) of the blood. Said testing means may be present at, e.g., a “test site” or an “analytical site.”

“Lancet” means any sharp member used to puncture the skin for the purpose of cutting blood vessels and allowing blood to flow to the surface of the skin. The lancet

has certain parameters such as diameter or width to define the cross-sectional area of the member, and geometry to define the shape of the distal or front lancing end of the member. "Lancet driver" means any means for propelling the lancet to puncture the skin. Examples of lancets and lancet drivers are well known in the art and are described
5 herein with relation to the invention.

Miniaturized lancing and actuator system

Referring to Figure 1, a blood sampling system incorporating a disposable sample acquisition module 100, a lancet driver 102, and an optional accessory module 104 are shown. The optional accessory module comprises a case body 106 having a storage
10 cavity 108 for storing sample acquisition modules 100. A cover to this cavity has been left out for clarity. The accessory module further comprises a chamber 110 for holding the lancet driver 102. The lancet driver has a preload adjustment knob 112, by which the trigger point of the lancet driver may be adjusted. This insures a reproducible tension on the surface of the skin for better control of the depth of penetration and blood
15 yield. In one embodiment, the sample acquisition module 100 is removably attached to the lancet driver 102, as shown, so that the sample acquisition module 100 is disposable and the lancet driver 102 is reusable. In an alternative embodiment, the sample acquisition module and lancet driver are contained within a single combined housing, and the combination sample acquisition module/lancet driver is disposable. The sample
20 acquisition module 100 includes a sampling site 114, preferably having a concave depression 116, or cradle, to conform to the shape of a user's finger or other anatomical feature (not shown). The sampling site further includes an opening 118 located in the concave depression. The lancet driver 102 is used to fire a lancet contained within and guided by the sample acquisition module 100 to create an incision on the user's finger
25 when the finger is placed on the sampling site 114. In one embodiment, the sampling site forms a substantially airtight seal at the opening when the skin is firmly pressed against the sampling site; the sampling site may additionally have a soft, compressible material surrounding the opening to further limit contamination of the blood sample by ambient air. "Substantially airtight" in this context means that only a negligible amount
30 of ambient air may leak past the seal under ordinary operating conditions, the substantially airtight seal allowing the blood to be collected seamlessly.

Figure 2 shows some details of one embodiment of the sample acquisition module. Figure 2A is a cross section view through line A of Figure 2B. The lancet 200 is protected in the integrated housing 202 that provides a cradle 204 for positioning the user's finger or other body part, a sampling port 206 within the cradle 204, and a sample reservoir 208 for collecting the resulting blood sample. The lancet 200 is a shaft with a distal end 210 sharpened to produce the incision with minimal pain. The lancet 200 further has an enlarged proximal end 212 opposite the distal end. Similar lancets are commonly known in the art. Rather than being limited to a shaft having a sharp end, the lancet may have a variety of configurations known in the art, with suitable modifications being made to the system to accommodate such other lancet configurations, such configurations having a sharp instrument that exits the sampling port to create a wound from which a blood sample may be obtained. In the figure, the lancet 200 is slidably disposed within a lancet guide 214 in the housing 202, and movement of the lancet 200 within the lancet guide 214 is closely controlled to reduce lateral motion of the lancet, thereby reducing the pain of the lance stick. The sample acquisition module also includes a return stop 228 which retains the lancet within the sample acquisition module. The sample acquisition module has an attachment site 232 for attachment to the lancet driver.

The sample acquisition module further includes a depth selector allowing the user to select one of several penetration depth settings. In Figure 2, the depth selector is shown as a multi-position thumbwheel 216 having a graduated surface. By rotating the thumbwheel 216, the user selects which part of the graduated surface contacts the enlarged proximal end 212 of the lancet to limit the movement of the lancet 200 within the lancet guide 214. The thumbwheel is maintained in the selected position by a retainer 218 having a protruding, rounded surface which engages at least one of several depressions 220 (e.g. dimples, grooves, or slots) in the thumbwheel 216. The depressions 220 are spatially aligned to correspond with the graduated slope of the thumbwheel 216, so that, when the thumbwheel 216 is turned, the depth setting is selected and maintained by the retainer 218 engaging the depression 220 corresponding to the particular depth setting selected. In alternate embodiments, the retainer may be located on the depth selector and the depressions corresponding to the depth setting located on the housing

such that retainer may functionally engage the depressions. Other similar arrangements for maintaining components in alignment are known in the art and may be used. In further alternate embodiments, the depth selector may take the form of a wedge having a graduated slope which contacts the enlarged proximal end of the lancet, with the wedge being retained by a groove in the housing.

The sample reservoir 208 includes an elongate, rounded chamber 222 within the housing 202 of the sample acquisition module. The chamber 222 has a flat or slightly spherical shape, with at least one side of the chamber 222 being formed by a smooth polymer, preferably absent of sharp corners. The sample reservoir 208 also includes an entrance 224 to the chamber 222, which is in fluid communication with the sampling port 206, and a vent 226 exiting the chamber. A cover (not shown), preferably of clear material such as plastic, positions the lancet 200 and closes the chamber 208, forming an opposing side of the chamber 208. In embodiments where the cover is clear, the cover may serve as a testing means whereby the sample may be analyzed in the reservoir via optical sensing techniques operating through the cover. A clear cover will also aid in determining by inspection when the sample reservoir is full of the blood sample.

Figure 3 shows a portion of the sample acquisition module illustrating an alternate embodiment of the sample reservoir. The sample reservoir has a chamber 300 having an entrance 302 joining the chamber 300 to a blood transport capillary channel 304; the chamber 300 also has a vent 306. The chamber has a first side 308 that has a flat or slightly spherical shape absent of sharp corners and is formed by a smooth polymer. An elastomeric diaphragm 310 is attached to the perimeter of the chamber 300 and preferably is capable of closely fitting to the first side of the chamber 308. To control direction of blood flow, the sample reservoir is provided with a first check valve 312 located at the entrance 302 of the sample reservoir and a second check valve 314 leading to an exit channel 316 located at the vent 306. Alternately, a single check valve (at the location 312) may be present controlling both flow into the chamber 300 via the blood transport capillary channel 304 and flow out of the chamber 300 into an optional alternate exit channel 318. The sample reservoir has a duct 320 connecting to a source of variable pressure facilitating movement of the diaphragm 310. When the diaphragm 310 is flexed away from the first side of the chamber 308 (low pressure supplied from

the source via duct 320), the first check valve 312 is open and the second check valve 314 is closed, aspiration of the blood sample into the sample reservoir follows. When the diaphragm 310 is flexed in the direction of the first side of the chamber 308 (high pressure supplied from the source via duct 320) with the first check valve 312 closed and the second check valve 314 open, the blood is forced out of the chamber 300. The direction of movement and actuation speed of the diaphragm 310 can be controlled by the pressure source, and therefore the flow of the sample can be accelerated or decelerated. This feature allows not only reduced damage to the blood cells but also for the control of the speed by which the chamber 300 is filled. While control of the diaphragm 310 via pneumatic means is described in this embodiment, mechanical means may alternately be used. Essentially, this micro diaphragm pump fulfills the aspiration, storage, and delivery functions. The diaphragm 310 may be used essentially as a pump to facilitate transfer of the blood to reach all areas required. Such required areas might be simple sample storage areas further downstream for assaying or for exposing the blood to a chemical sensor or other testing means. Delivery of the blood may be to sites within the sample acquisition module or to sites outside the sample acquisition module, i.e. a separate analysis device. In an alternate embodiment, a chemical sensor or other testing means is located within the sample acquisition module, and the blood is delivered to the chemical sensor or other testing means via a blood transfer channel in fluid communication with the sample reservoir. The components of the sample acquisition module may be injection molded and the diaphragm may be fused or insertion molded as an integral component.

Figure 4 depicts a portion of the disposable sample acquisition module surrounding the sampling port 400, including a portion of the sampling site cradle surface 402. The housing of the sample acquisition module includes a primary capillary channel 404 connecting the sampling port to the sample reservoir. The primary capillary channel 404 includes a primary channel luminal surface 406 and a primary channel entrance 408, the primary channel entrance 408 opening into the sampling port 400. The sample acquisition module may optionally include a supplemental capillary channel 410 having a supplemental channel luminal surface 412 and a supplemental channel entrance 414, the supplemental channel entrance 414 opening into the sampling port 400. The

primary capillary channel 404 has a greater cross-sectional area than the supplemental capillary channel 410, preferably by at least a factor of two. Thus, the supplemental capillary channel 410 draws fluid faster than the primary capillary channel 404. When the first droplet of blood is received into the sampling port 400, the majority of this droplet is drawn through the supplemental capillary channel 410. However, as the blood continues to flow from the incision into the sampling port 400, most of this blood is drawn through the primary capillary channel 404, since the supplemental capillary channel 410 is of limited capacity and is filled or mostly filled with the first blood droplet. This dual capillary channel configuration is particularly useful in testing where there is a concern with contamination of the sample, e.g. with debris from the lancet strike or (particularly in the case of blood gas testing) with air.

In order to improve blood droplet flow, some priming or wicking of the surface with blood is at times necessary to begin the capillary flow process. Portions of the surfaces of the sampling port 400 and the primary and supplemental (if present) capillary channels 404, 410 are treated to render those surfaces hydrophilic. The surface modification may be achieved using mechanical, chemical, corona, or plasma treatment. Examples of such coatings and methods are marketed by AST Products (Billerica, MA) and Spire Corporation (Bedford, MA). However, a complete blanket treatment of the surface could prove detrimental by causing blood to indiscriminately flow all over the surface and not preferentially through the capillary channel(s). This ultimately will result in losses of blood fluid. The particular surfaces which receive the treatment are selected to improve flow of blood from an incised finger on the sampling site cradle surface 402 through the sampling port 400 and at least one of the capillary channels 404, 410 to the sample reservoir. Thus, the treatment process should be masked off and limited only to the selected surfaces. The masking process of selectively modifying the sampling surface from hydrophobic to hydrophilic may be done with mechanical masking techniques such as with metal shielding, deposited dielectric or conductive films, or electrical shielding means. In some embodiments, the treated surfaces are limited to one or more of the following: the surface of the sampling port which lies between the sampling site cradle surface and the primary and supplemental capillary channel, the surface immediately adjacent to the entrances to the primary and/or

supplemental capillary channels 408, 414 (both within the sampling port and within the capillary channel), and the luminal surface of the primary and/or supplemental capillary channels 406, 412. The blood upon exiting the incision preferentially moves through the sampling port 400 into the supplementary capillary channel 410 (if present) and into the primary capillary channel 404 to the sample reservoir, resulting in efficient capture of the blood. Alternatively, the substrate material may be selected to be hydrophilic or hydrophobic, and a portion of the surface of the substrate material may be treated for the opposite characteristic.

Still looking at Figure 4, in a preferred embodiment, a membrane 416 at the base of the sampling port 400 is positioned between the retracted sharpened distal end of the lancet 418 and the entrance to the capillary channels 408, 414. The membrane 416 facilitates the blood sample flow through the capillary channels 404, 410 by restricting the blood from flowing into the area 418 surrounding the distal end of the lancet 420. The blood thus flows preferentially into the sample reservoir. In an embodiment, the membrane 416 is treated to have a hydrophobic characteristic. In another embodiment, the membrane 416 is made of polymer-based film 422 that has been coated with a silicone-based gel 424. For example, the membrane structure may comprise a polymer-based film 422 composed of polyethylene terephthalate, such as the film sold under the trademark MYLAR. The membrane structure may further comprise a thin coating of a silicone-based gel 424 such as the gel sold under the trademark SYLGARD on at least one surface of the film. The usefulness of such a film is its ability to reseal after the lancet has penetrated it without physically affecting the lancet's cutting tip and edges. The MYLAR film provides structural stability while the thin SYLGARD silicone laminate is flexible enough to retain its form and close over the hole made in the MYLAR film. Other similar materials fulfilling the structural stability and flexibility roles may be used in the manufacture of the membrane in this embodiment.

The membrane 416 operates to allow the sharpened distal end of the lancet 420 to pierce the membrane as the sharpened distal end of the lancet 420 travels into and through the sampling port 400. In the most preferred embodiment, the silicone-based gel 424 of the membrane 416 automatically seals the cut caused by the piercing lancet. Therefore, after an incision is made on a finger of a user, the blood from the incision

is prevented from flowing through the membrane 416, which aids the blood to travel through the primary capillary channel 404 to accumulate within the sample reservoir. Thus the film prevents any blood from flowing into the lancet device assembly, and blood contamination and loss into the lancet device mechanism cavity are prevented.

5 Even without the resealing layer 424, the hydrophobic membrane 416 deters the flow of blood across the membrane 416, resulting in improved flow through the primary capillary channel 404 and reduced or eliminated flow through the pierced membrane 416.

Figures 5A, 5B, and 5C illustrate one implementation of the lancet driver at three different points during the use of the lancet driver. In this description of the lancet driver, proximal indicates a position relatively close to the site of attachment of the sample acquisition module; conversely, distal indicates a position relatively far from the site of attachment of the sample acquisition module. The lancet driver has a driver handle body 500 defining a cylindrical well 502 within which is a preload spring 504.

10 Proximal to the preload spring 504 is a driver sleeve 506 which closely fits within and is slidably disposed within the well 502. The driver sleeve 506 defines a cylindrical driver chamber 508 within which is an actuator spring 510. Proximal to the actuator spring 510 is a plunger sleeve 512 which closely fits within and is slidably disposed within the driver sleeve 506.

The driver handle body 500 has a distal end 514 defining a threaded passage 516 into which a preload screw 518 fits. The preload screw defines a counterbore 520. The preload screw 518 has a distal end 522 attached to a preload adjustment knob 524 and a proximal end 526 defining an aperture 528. The driver sleeve 506 has a distal end 530 attached to a catch fitting 532. The catch fitting 532 defines a catch hole 534. The driver sleeve 506 has a proximal end 536 with a sloped ring feature 538 circling the interior surface of the driver sleeve's proximal end 536.

20

25

The lancet driver includes a plunger stem 538 having a proximal end 540 and a distal end 542. At its distal end 542, the plunger stem 538 is terminated by an enlarged plunger head 544. At its proximal end 540, the plunger stem 538 is terminated by an enlarged plunger base 546. A plunger hook 548 is located on the plunger stem 538 between the plunger head 544 and the plunger base 546. The plunger base 546 is

30

fixedly attached to the plunger sleeve 512, and the plunger head 544 is slidably disposed within the counterbore 520 defined by the preload screw 518. The plunger stem 538 extends from the plunger head 544, through the aperture 528 defined by the proximal end 526 of the preload screw, thence through the hole 534 in the catch fitting 532, to the plunger base 546. The plunger base 546 extends proximally past the plunger sleeve 512 to form a plunger tip 550. For assembly purposes, the plunger base 546 may be incorporated into the plunger sleeve 512, and the plunger stem 538 attached to the plunger base 546 by crimping, swaging, gluing, welding, or some other means.

The operation of the blood sampling system may be described as follows, with reference to Figures 1 through 5. In operation, a fresh sample acquisition module 100 is removed from the storage cavity 108 and adjusted for the desired depth setting using the multi-position thumbwheel 216. The sample acquisition module 100 is then placed onto the end of the lancet driver 102. The preload setting may be checked, but will not change from cycle to cycle once the preferred setting is found; if necessary, the preload setting may be adjusted using the preload adjustment knob 112. The combined sample acquisition module and lancet driver assembly is then pressed against the user's finger (or other selected anatomical feature) in a smooth motion until the preset trigger point is reached. The trigger point corresponds to the amount of preload force that needs to be overcome to actuate the driver to drive the lancet towards the skin. The preload screw allows the preload setting to be adjusted by the user such that a consistent, preset (by the user) amount of preload force is applied to the sampling site 114 each time a lancing is performed.

When the motion to press the assembly against the user's finger is begun (see Figure 5A), the plunger hook 548 engages catch fitting 532, holding the actuator spring 510 in a cocked position while the force against the finger builds as the driver sleeve 506 continues to compress the preload spring 504. Eventually (see Figure 5B) the sloped back of the plunger hook 548 slides into the hole 528 in the proximal end of the preload screw 526 and disengages from the catch fitting 532. The plunger sleeve 512 is free to move in a proximal direction once the plunger hook 548 releases, and the plunger sleeve 512 is accelerated by the actuator spring 510 until the plunger tip 550 strikes the enlarged proximal end of the lancet 212. Upon striking the enlarged proximal

end of the lancet 212, the plunger tip 550 of the actuated lancet driver reversibly engages the enlarged proximal end of the lancet 212. This may be accomplished by mechanical means, e.g. a fitting attached to the plunger tip 550 that detachably engages a complementary fitting on the enlarged proximal end of the lancet 212, or the enlarged proximal end of the lancet 212 may be coated with an adhesive that adheres to the plunger tip 550 of the actuated lancet driver. Upon being engaged by the plunger tip 550, the lancet 200 slides within the lancet guide 214 with the sharpened distal end of the lancet 210 emerging from the housing 202 through the sampling port 206 to create the incision in the user's finger. At approximately the point where the plunger tip 550 contacts the enlarged proximal end of the lancet 212, the actuator spring 510 is at its relaxed position, and the plunger tip 550 is traveling at its maximum velocity. During the extension stroke, the actuator spring 510 is being extended and is slowing the plunger tip 550 and lancet 200. The end of stroke occurs (see Figure 5C) when the enlarged proximal end of the lancet 212 strikes the multi-position thumbwheel 216. The direction of movement of the lancet 200 is reversed and the extended actuator spring then quickly retracts the sharpened distal end of the lancet 210 back through the sampling port 206. At the end of the return stroke, the lancet 200 is stripped from the plunger tip 550 by the return stop 228. The adhesive adheres to the return stop 228 retaining the lancet in a safe position.

As blood seeps from the wound, it fills the sampling port 206 and is drawn by capillary action into the sample reservoir 208. In this embodiment, there is no reduced pressure or vacuum at the wound, i.e. the wound is at ambient air pressure, although embodiments which draw the blood sample by suction, e.g. supplied by a syringe or pump, may be used. The vent 226 allows the capillary action to proceed until the entire chamber is filled, and provides a transfer port for analysis of the blood by other instrumentation. The finger is held against the sample acquisition module until a complete sample is observed in the sample reservoir. As the sample acquisition module 100 is removed from the lancet driver 102, a latch 230 that is part of the return stop 228 structure engages a sloped ring feature 538 inside the lancet driver 102. As the lancet driver 102 is removed from the sample acquisition module 100, the latch forces the

return stop 228 to rotate toward the lancet 200, bending it to lock it in a safe position, and preventing reuse.

As the sample acquisition module 100 is removed from the lancet driver 102, the driver sleeve 506 is forced to slide in the driver handle body 500 by energy stored in the preload spring 504. The driver sleeve 506, plunger sleeve 512, and actuator spring 510 move outward together until the plunger head 544 on the plunger stem 538 contacts the bottom of the counterbore 520 at the proximal end of the preload screw 526. The preload spring 504 continues to move the driver sleeve 506 outward compressing the actuator spring 510 until the plunger hook 548 passes through the hole 534 in the catch fitting 532. Eventually the two springs reach equilibrium and the plunger sleeve 512 comes to rest in a cocked position.

After the sample acquisition module 100 is removed from the lancet driver 102, it may be placed in a separate analysis device to obtain blood chemistry readings. In a preferred embodiment, the integrated housing 202 or sample reservoir 208 of the sample acquisition module 100 contains at least one biosensor which is powered by and/or read by the separate analysis device. In another embodiment, the analysis device performs an optical analysis of the blood sample directly through the clear plastic cover of the sample acquisition module. Alternatively, the blood sample may be transferred from the sample acquisition module into an analysis device for distribution to various analysis processes.

Alternate embodiments of the invention offer improved success rates for sampling, which reduces the needless sacrifice of a sample storage reservoir or an analysis module due to inadequate volume fill. Alternate embodiments allow automatic verification that sufficient blood has been collected before signaling the user (e.g. by a signal light or an audible beep) that it is okay to remove the skin from the sampling site. In such alternate embodiments, one or more additional lancet(s) (denoted backup lancets) and/or lancet driver(s) (denoted backup lancet drivers) and/or sample reservoir(s) (denoted backup sample reservoirs) are present with the "primary" sample acquisition module. In one such preferred embodiment, following detection of inadequate blood sample volume (e.g., by light or electronic methods), a backup sampling cycle is initiated automatically. The "backup sampling cycle" includes disconnecting the primary

sample reservoir via a simple valving system, bringing the backup components online, lancing of the skin, collection of the blood, and movement of the blood to the backup sample reservoir. Blood flows into the backup sample reservoir until the required volume is obtained. The cycle repeats itself, if necessary, until the correct volume is obtained. Only then is the sample reservoir made available as a source of sampled blood for use in measurements or for other applications. The series of reservoirs and/or lancets and/or lancet drivers may easily be manufactured in the same housing and be transparent to the user. In one embodiment, up to three sample reservoirs (the primary plus two backup) are present in a single sample acquisition module, each connected via a capillary channel/valving system to one or more sampling ports. Another embodiment has four sample reservoirs (the primary plus three backup) present in a single sample acquisition module, each connected via a capillary channel/valving system to one or more sampling ports. With three or four sample reservoirs, at least an 80% sampling success rate can be achieved for some embodiments.

Another embodiment includes a miniaturized version of the lancet device. Several of the miniature lancets may be located in a single sampling site, with corresponding capillary channels to transfer blood to one or more reservoirs. The capillary channels may optionally have valves for controlling flow of blood. The device may also include one or more sensors for detecting the presence of blood, e.g. to determine if a sufficient quantity of blood has been obtained. In such an embodiment, the combined blood sampling system - the disposable sample acquisition module, the lancet driver, and the optional accessory module will have dimensions no larger than about 150 mm long, 60 mm wide, and 25 mm thick. In other embodiments, the size of the combined blood sampling system including the disposable sample acquisition module, the lancet driver, and the optional accessory module will have dimensions no larger than about 100 mm long, about 50 mm wide, and about 20 mm thick, and in still other embodiments no larger than about 70 mm long, about 30 mm wide, and about 10 mm thick. The size of the combined blood sampling system including the disposable sample acquisition module, the lancet driver, and the optional accessory module will generally be at least about 10 mm long, about 5 mm wide, and about 2 mm thick.

In another miniature embodiment, the dimensions of the lancet driver without the accessory module or sample acquisition module are no larger than about 80 mm long, 10 mm wide, and 10 mm thick, or specifically no larger than about 50 mm long, 7 mm wide, and 7 mm thick, or even more specifically no larger than about 15 mm long, 5 mm wide, and 3 mm thick; dimensions of the lancet driver without the accessory module or sample acquisition module are generally at least about 1 mm long, 0.1 mm wide, and 0.1 mm thick, or specifically at least about 2 mm long, 0.2 mm wide, and 0.2 mm thick, or more specifically at least about 4 mm long, 0.4 mm wide, and 0.4 mm thick. In yet another miniature embodiment, dimensions of the miniature sample acquisition module without the lancet driver or accessory module are no larger than about 15 mm long, about 10 mm wide, and about 10 mm thick, or no larger than about 10 mm long, about 7 mm wide, and about 7 mm thick, or no larger than about 5 mm long, about 3 mm wide, and about 2 mm thick; dimensions of the miniature sample acquisition module without the lancet driver or accessory module are generally at least about 1 mm long, 0.1 mm wide, and 0.1 mm thick, specifically at least about 2 mm long, 0.2 mm wide, and 0.2 mm thick, or more specifically at least about 4 mm long, 0.4 mm wide, and 0.4 mm thick.

In another embodiment, the miniaturized sample acquisition module and the lancet driver form a single unit having a shared housing, and the combined sample acquisition module/lancet driver unit is disposable. Such a combined unit is no larger than about 80 mm long, about 30 mm wide, and about 10 mm thick, specifically no larger than about 50 mm long, about 20 mm wide, and about 5 mm thick, more specifically, no larger than about 20 mm long, about 5 mm wide, and about 3 mm thick; the combined unit is generally at least about 2 mm long, about 0.3 mm wide, and about 0.2 mm thick, specifically at least about 4 mm long, 0.6 mm wide, and 0.4 mm thick, more specifically, at least about 8 mm long, 1 mm wide, and 0.8 mm thick.

Although the above-described embodiments of the present invention have been described in detail, various modifications to the present invention will become apparent to those skilled in the art from the foregoing description and accompanying drawings and will be within the scope of the invention, which is to be limited only by the following claims.

CLAIMS

1. A device for collecting blood from the skin of a patient, the device comprising

a housing having a sampling site, the sampling site defining an opening,
a sample reservoir in fluid communication with the opening,

5 a lancet maintained within the housing, the lancet having a lancet tip adjacent the opening, and

a lancet driver operably disposed to the lancet to drive the lancet tip through the opening to lance the skin when the lancet driver is actuated,

10 the device being configured to allow actuation of the lancet driver, lancing of the skin, collection of the blood, and movement of the blood to the sample reservoir to be integrated,

the device further being configured to allow the blood to be collected seamlessly.

2. The device of claim 1, wherein the sampling site is adapted to conform
15 to the skin of the patient to form a substantially airtight seal at the opening when the skin is firmly pressed against the sampling site.

3. The device of claim 1, further comprising a sampling port and a pierceable membrane, the sampling port having a first end contiguous with the opening and a second end opposite the first end relatively nearer to the lancet tip than the first
20 end, the pierceable membrane adjacent to the second end between the lancet tip and the opening.

4. The device of claim 3, wherein the membrane is resealable.

5. The device of claim 3, wherein the sampling port has a surface, wherein at least a portion of the sampling port surface is hydrophilic.

6. The device of claim 3, wherein the membrane has a surface, wherein at least a portion of the membrane surface is hydrophobic.

7. The device of claim 1, further comprising at least one capillary channel in fluid communication with the opening and the sample reservoir, the capillary channel
5 having a surface, at least a portion of the capillary channel surface being hydrophilic.

8. The device of claim 7, having at least two capillary channels, wherein at least one of the capillary channels is a primary capillary channel and at least one of the capillary channels is a supplemental capillary channel, each capillary channel having a cross-sectional area, wherein the cross-sectional area of the at least one primary capillary
10 channel is at least twice the cross sectional area of the at least one supplemental capillary channel.

9. The device of claim 7, wherein the sample reservoir comprises a chamber in fluid communication with the opening, the chamber having a perimeter, and a flexible diaphragm attached to the perimeter of the chamber, the flexible diaphragm capable of
15 moving within the chamber under the influence of a pressure source, said movement of the diaphragm serving to facilitate transport of the blood through the at least one capillary channel.

10. The device of claim 1, wherein the device further comprises testing means in fluid communication with the opening.

20 11. The device of claim 1, further comprising a depth selector in operable relation to the lancet and a preload adjustment means in operable relation to the lancet driver.

12. The device of claim 1, wherein the device has dimensions smaller than about 80 mm by 30 mm by 10 mm.

-20-

13. The device of claim 1, further comprising a backup lancet operably disposed to the sampling site.

14. The device of claim 1, further comprising a backup lancet having a backup lancet tip, the backup lancet maintained within the housing, the sampling site defining
5 a backup opening adjacent the backup lancet tip, the backup opening in fluid communication with the sample reservoir.

15. The device of claim 1, further comprising a backup reservoir in fluid communication with the sampling site.

16. The device of claim 1, further comprising a backup lancet having a backup
10 lancet tip, the backup lancet maintained within the housing, the sampling site defining a backup opening adjacent the backup lancet tip, the sample acquisition module further comprising a backup reservoir in fluid communication with the backup opening.

17. A sample acquisition module for use in collecting blood from the skin of a patient, the sample acquisition module comprising

15 a housing,
a sampling site on the housing defining an opening, the sampling site shaped to conform to the skin and to form a substantially airtight seal with the skin,

a lancet maintained within the housing, the lancet having a lancet tip adjacent the opening, wherein the lancet is operable to send the lancet tip through the opening to
20 lance the skin of the patient, and

a sample reservoir in fluid communication with the opening,
the sample acquisition module configured to allow
seamless sampling of the blood, and

a)
25 integrated lancing of the skin, collection of the blood through the opening, and movement of the blood to the sample reservoir.

18. The sample acquisition module of claim 17, wherein the housing further comprises an attachment site for attaching a lancet driver.

5 19. The sample acquisition module of claim 17, wherein the sample acquisition module further comprises a lancet driver within the housing, the lancet driver operably disposed to the lancet.

10 20. The sample acquisition module of claim 17, further comprising a sampling port and a pierceable membrane, the sampling port having a first end contiguous with the opening and a second end opposite the first end relatively nearer to the lancet tip than the first end, the pierceable membrane adjacent to the second end between the lancet tip and the opening.

21. The sample acquisition module of claim 20, wherein the membrane is resealable.

22. The sample acquisition module of claim 20, wherein the sampling port has a surface, wherein at least a portion of the sampling port surface is hydrophilic.

15 23. The sample acquisition module of claim 20, wherein the membrane has a surface, wherein at least a portion of the membrane surface is hydrophobic.

20 24. The sample acquisition module of claim 17, further comprising at least one capillary channel in fluid communication with the opening and the sample reservoir, the capillary channel having a surface, at least a portion of the capillary channel surface being hydrophilic.

25. The sample acquisition module of claim 24, having at least two capillary channels, wherein at least one of the capillary channels is a primary capillary channel and at least one of the capillary channels is a supplemental capillary channel, each capillary channel having a cross-sectional area, wherein the cross-sectional area of the

-22-

at least one primary capillary channel is at least twice the cross-sectional area of the at least one supplemental capillary channel.

26. The sample acquisition module of claim 24, wherein the sample reservoir comprises a chamber in fluid communication with the opening, the chamber having a perimeter, and a flexible diaphragm attached to the perimeter of the chamber, the flexible diaphragm capable of moving within the chamber under the influence of a pressure source, said movement of the diaphragm serving to facilitate transport of the blood through the at least one capillary channel.

27. The sample acquisition module of claim 17, further comprising testing means in fluid communication with the opening.

28. The sample acquisition module of claim 17, wherein the sample acquisition module has dimensions smaller than about 15 mm long, about 10 mm wide, and about 10 mm thick.

29. The sample acquisition module of claim 17, further comprising a backup lancet operably disposed to the sampling site.

30. The sample acquisition module of claim 17, further comprising a backup lancet having a backup lancet tip, the backup lancet maintained within the housing, the sampling site defining a backup opening adjacent the backup lancet tip, the backup opening in fluid communication with the sample reservoir.

31. The sample acquisition module of claim 17, further comprising a backup reservoir in fluid communication with the sampling site.

32. The sample acquisition module of claim 17, further comprising a backup lancet having a backup lancet tip, the backup lancet tip maintained within the housing, the sampling site defining a backup opening adjacent the backup lancet tip, the sample

acquisition module further comprising a backup reservoir in fluid communication with the backup sample opening.

33. A method of collecting blood from the skin of a patient, the method comprising

- 5 a) contacting the skin of the patient with a blood sampling device,
 b) performing a single initiating act resulting in the blood sampling device
lancing the skin, collecting blood from the skin, and moving blood to a storage reservoir
within the sampling device.

10 34. The method of claim 33, wherein the single initiating act also results in
analysis of the blood.

35. The method of claim 34, wherein the single initiating act also results in
display of information obtained from the analysis of the blood.

36. The method of claim 33, wherein the blood is collected and stored
seamlessly.

15 37. The method of claim 33, wherein the single initiating act also results in
verification that sufficient blood has been collected and, if insufficient blood has been
collected, a backup lancing cycle is initiated.

20 38. The method of claim 33, wherein the single initiating act also results in
verification that sufficient blood has been collected and, if sufficient blood has been
collected, signaling that the blood sampling device may be removed from contact with
the skin of the patient.

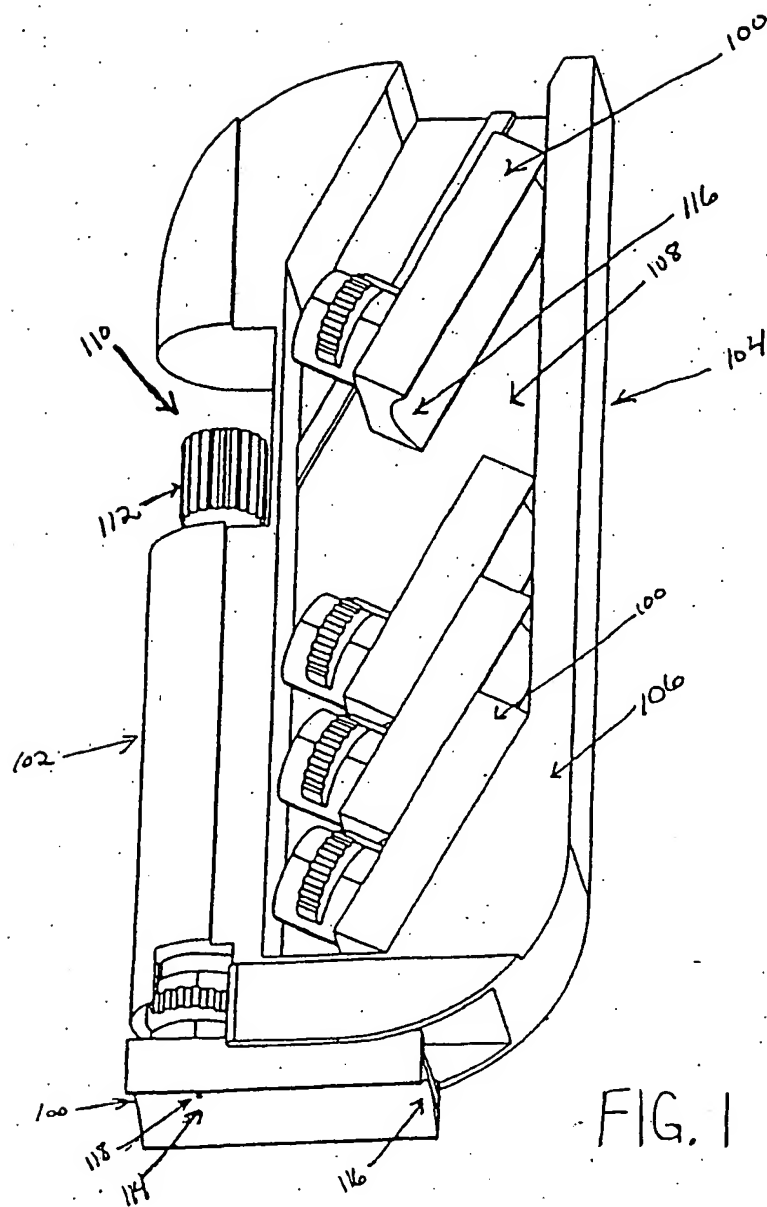


FIG. 1

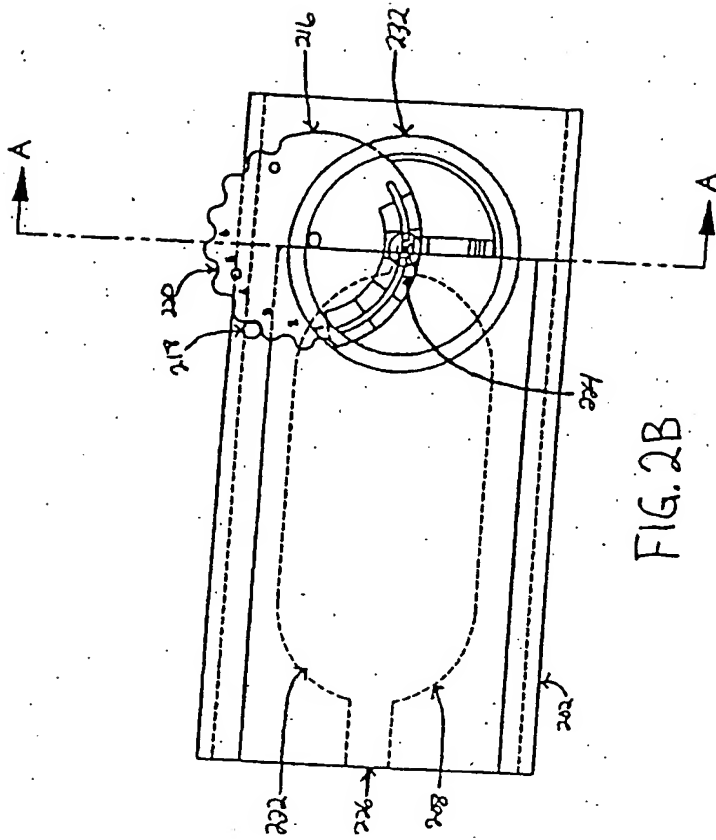


FIG. 2A

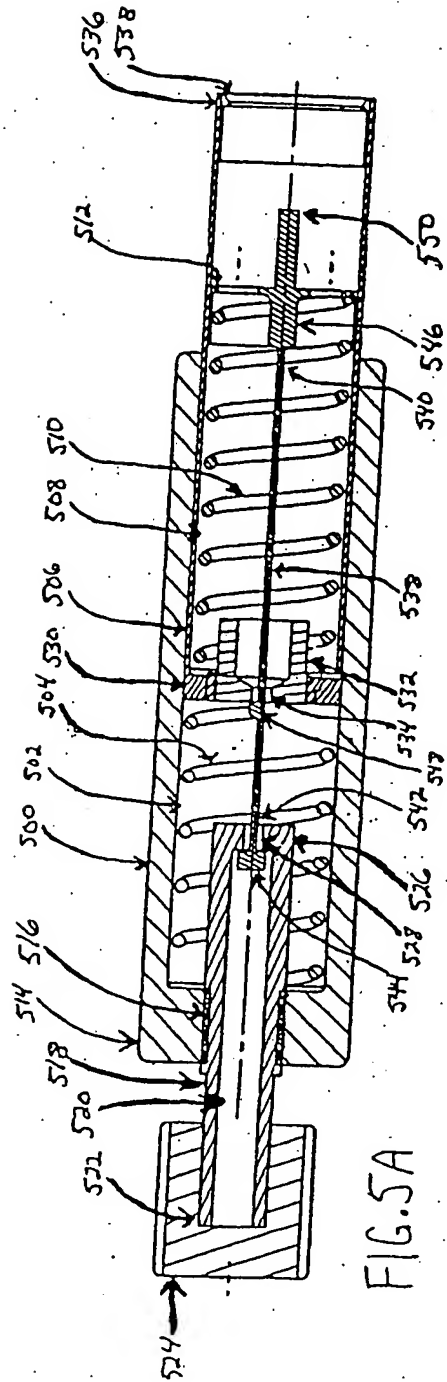


FIG. 2B

FIG. 5A

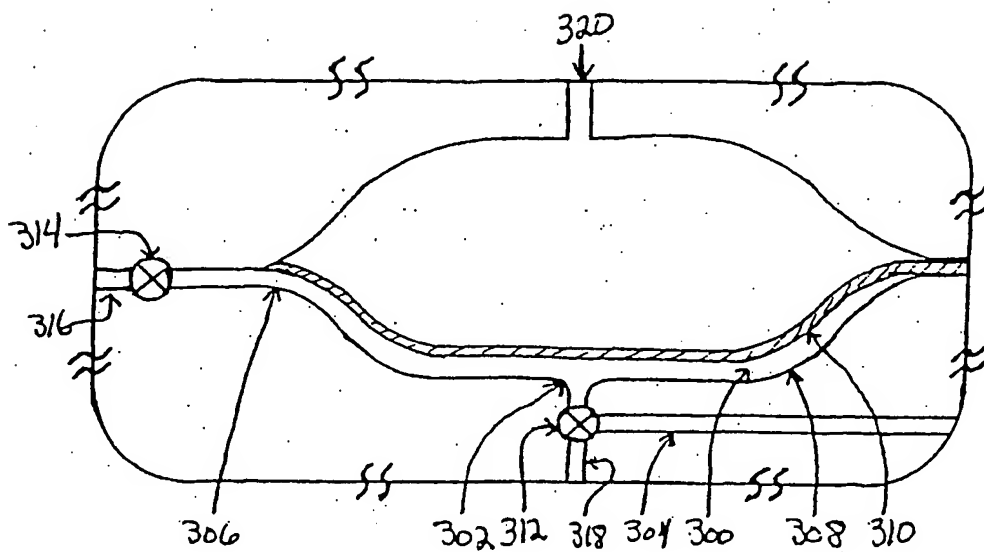


FIG. 3

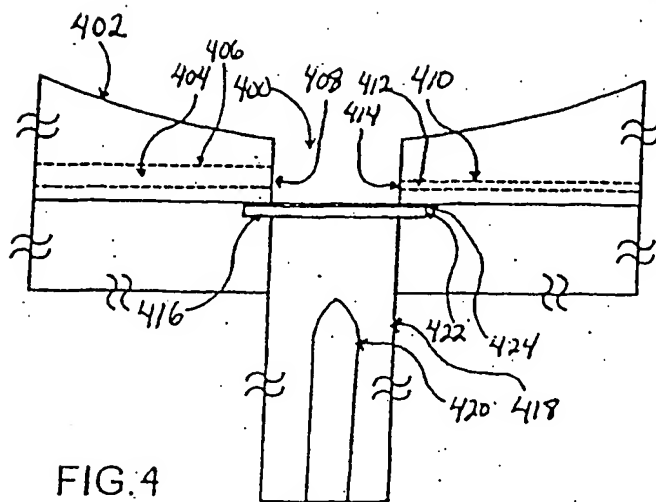


FIG. 4

